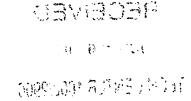
## FIG.\_1A

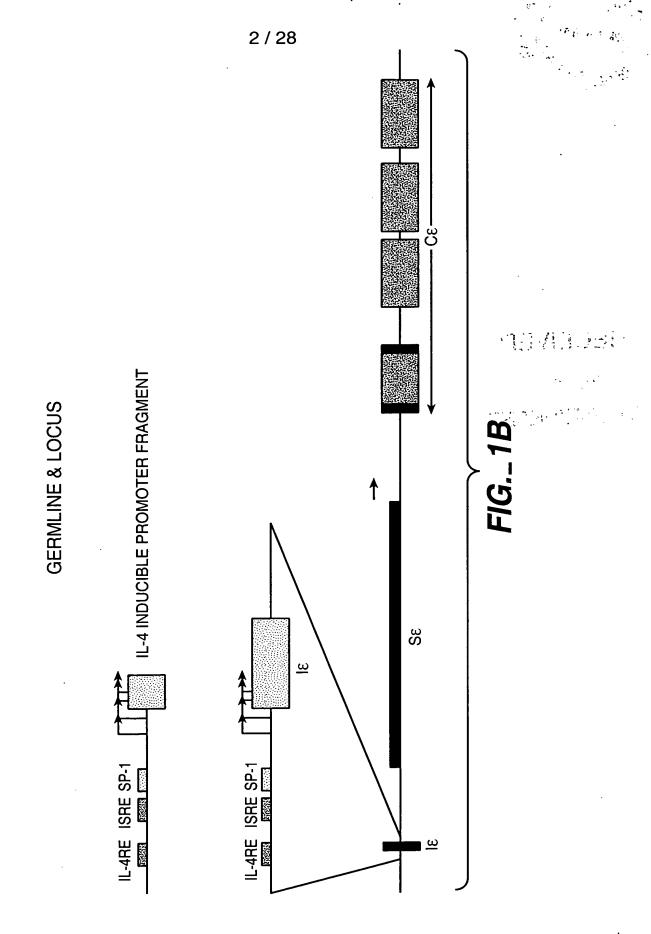


- 1 GCTGGGCTAA ACTGGGCTAG CCTGAGCTGG GCTGAACTGG GCTGCTGGGC
- 51 TGGACTGGGT AAGCTGGGCT GAGCTGGGTT GGGTGGAAAT GGGCTGAGCT

# FIG.\_2B

- 1 GGTTTGGCTG GGCTGGGCTG GGCTGGGCTG GGTTCAGCTG AGCGGGTTGG
- 51 GTTAGACTGG GTCAAACTGG TTCAGC

FIG.\_2C



-|-

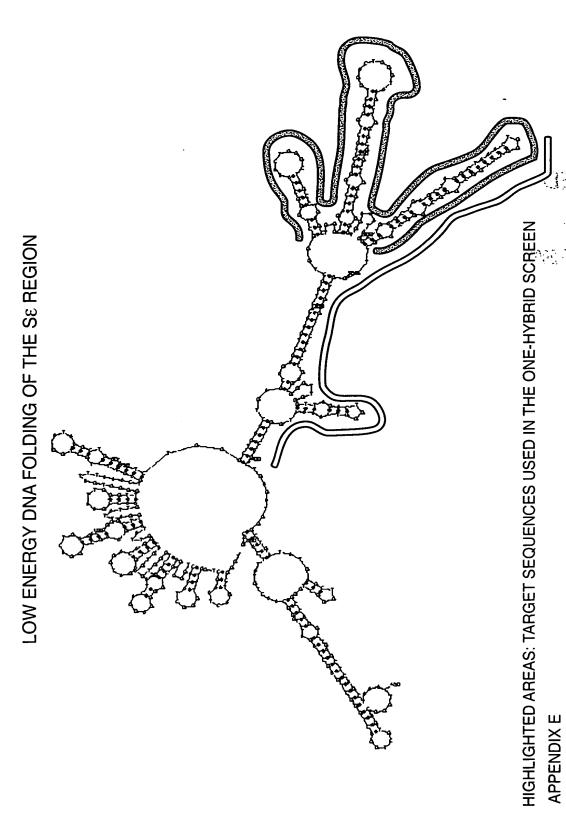
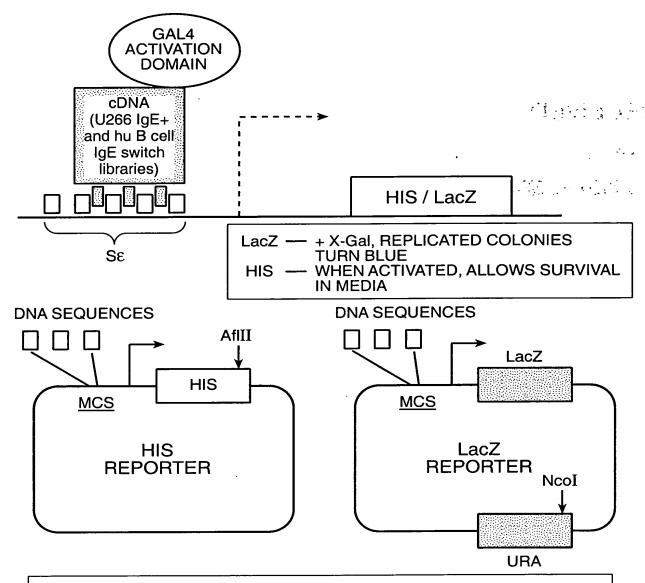


FIG.\_2A

### YEAST ONE-HYBRID SCREENING



### ONE HYBRID REPORTER VECTORS

DNA SEQUENCES OF INTEREST ARE INSERTED INTO THE MULTIPLE CLONING SITES (MCS).

THE ENZYME USED TO LINEARIZE THE VECTOR IS SHOWN WITH A SOLID ARROW.

DASHED ARROWS INDICATE THE TRANSCRIPTION OF THE REPORTER GENE.

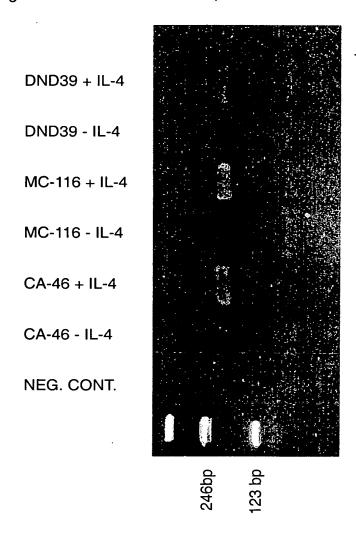
APPENDIX F

FIG.\_3

# IL-4 INDUCTION OF GERMLINE ε mRNA IN THE IgM + B CELL LINES: CA-46, MC-116 AND DND39

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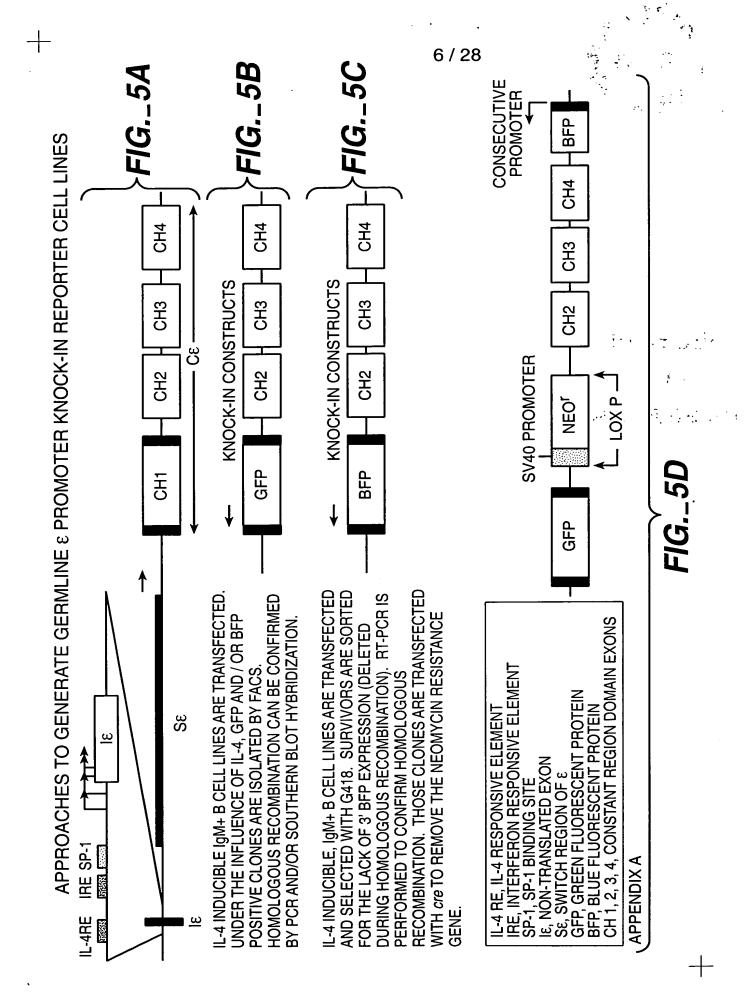
MEROPE CENTER OF



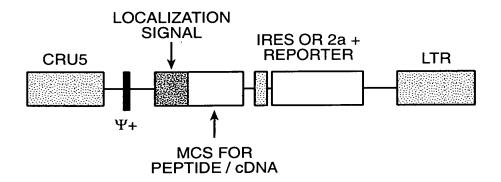
CELLS WERE INCUBATED FOR 48 HRS. IN 300 U / ml OF h-IL-4. RT-PCR WAS PERFORMED USING PRIMERS SPECIFIC FOR THE GERMLINE  $\epsilon$  EXON AND THE 5'-END OF THE C $\epsilon$  CH1 EXON (PREDICTED SIZE  $\sim$  200 bp).

FIG.\_4

APPENDIX G



### RIGEL BASE VECTOR

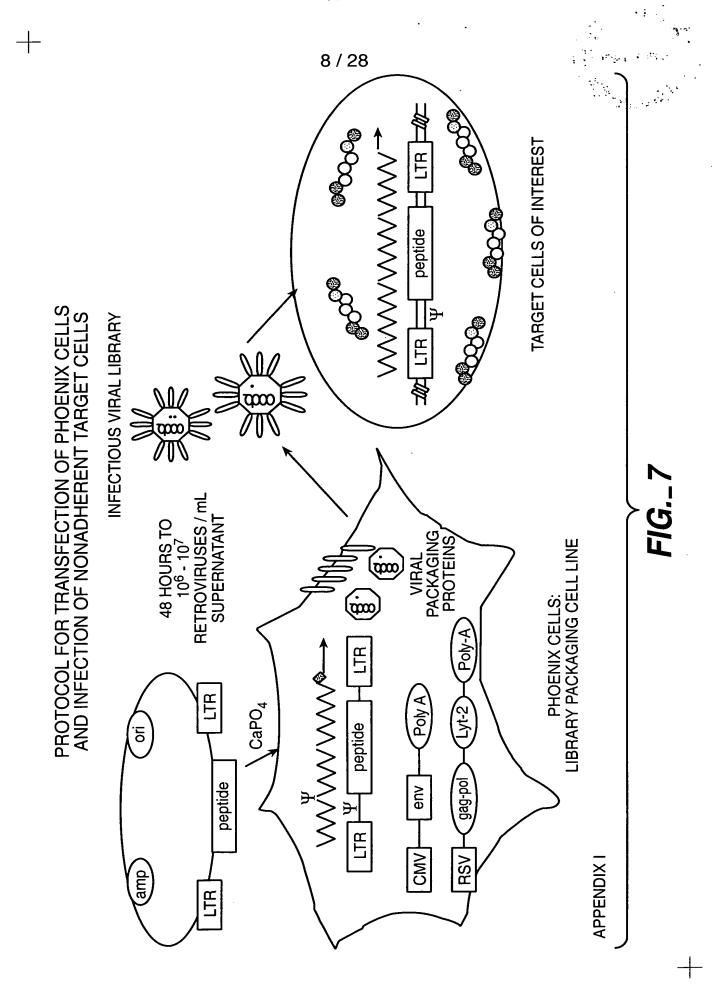


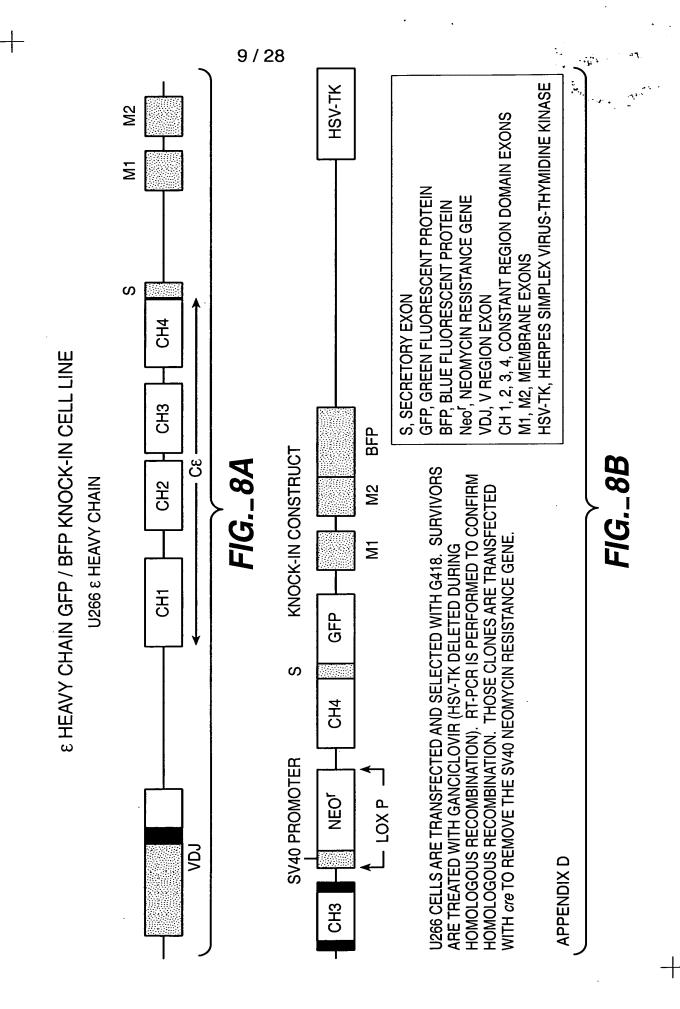
### ALL COMPONENTS ARE UNIQUELY CASSETTED FOR FLEXIBILITY

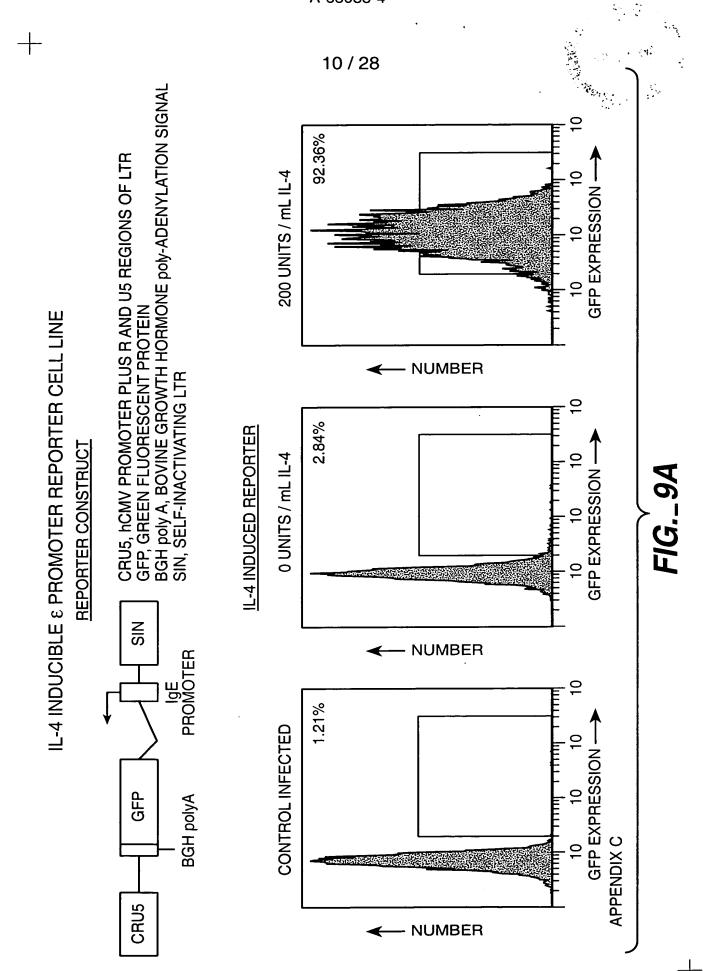
CRU5, MODIFIED LTR
LTR, LONG TERMINAL REPEAT
Y+, PACKING SIGNAL
LOCALIZATION SIGNAL: NUCLEAR, CELL MEMBRANE, GRANULAR
MCS, MULTIPLE CLONING SITE
IRES, INTERNAL RIBOSOME ENTRY SITE
2a, SELF-CLEAVING PEPTIDE

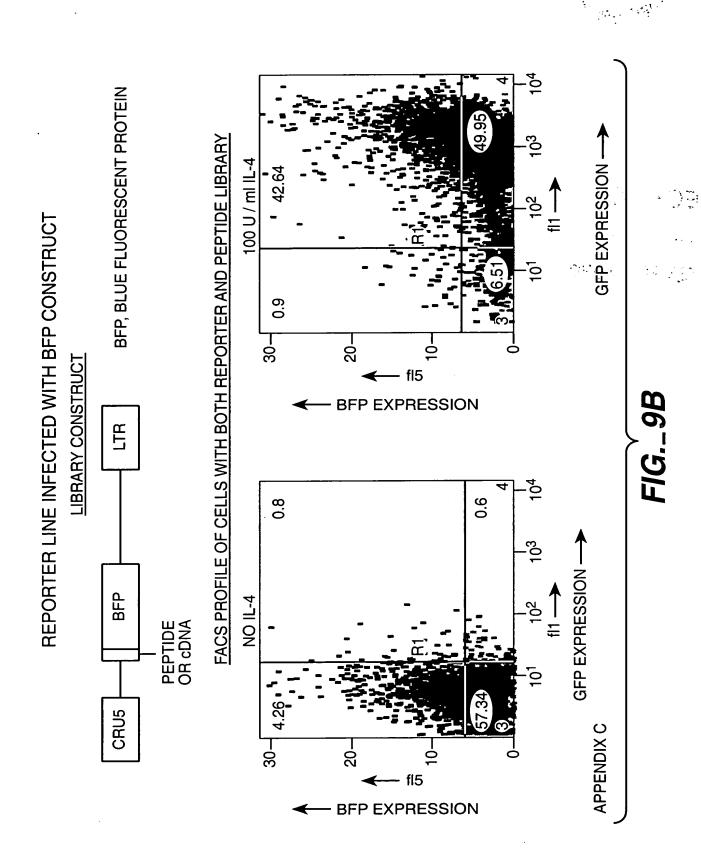
APPENDIX I

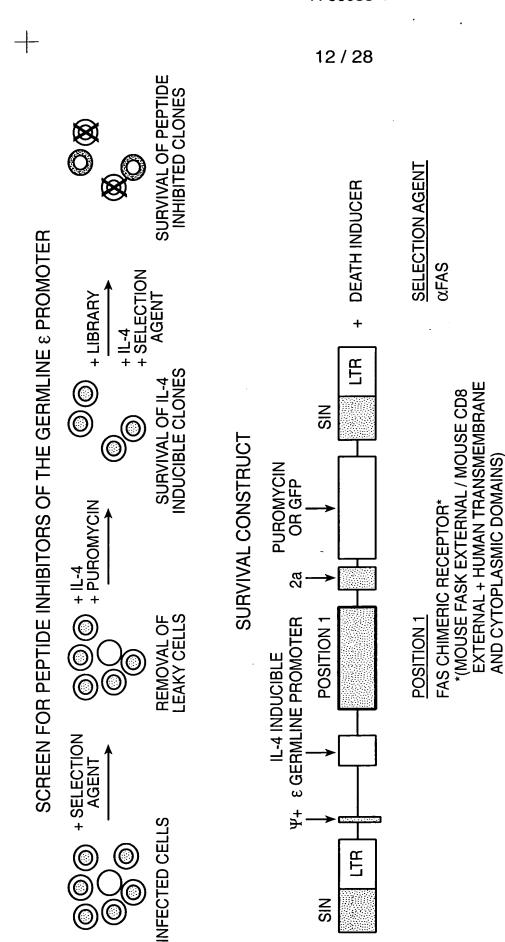
**FIG.\_6** 











APPENDIX D

ALL COMPONENTS ARE CASSETTED FOR FLEXIBILITY

p21 PEPTIDE

P450 2B1 HSV-TK

SIN, SELF-INACTIVATING LTR LTR, LONG TERMINAL REPEAT ) []

NONE (SELF SELECTION) CYCLOPHOSPHAMIDE

GANCICLOVIR

1-845 CMV promoter/R/U5 5' LTR

1322 GAG ATG-ATC mutation

850-2100 extended \( \psi\$ region

2146-2173 two Bstx1 peptide cloning sites

2205-2723 ECMV IRES (cloned as EcoR1/Msc1 fragment from pCITE-4a [Novagen])

2746-3465 GFP coding region

3522-4115 3' LTR

4122-6210 pGEM backbone (pUC origin, ampR)

**ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATCC** CAAACTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATCAA TTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAA **ATGGCCCGCCTGGCTGACCGCCCAACGACCCCCCGCCCATTGACGTCAATAATGACGTATG** TTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGT **AAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG** TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTC CTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTTGGC **AGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCA TTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA** ACAACTCCGCCCCATTGACGCAAATGGGCGTAGGCATGTACGGTGGGAGGTCTATATAA GCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACT GAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGT CTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTT CATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCACCGACCCACCACCG GGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCTAGTGTCTATGACTGA TTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGTATCTGGCGGACCCGTGG TGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAGACGTCCCAGGGACTTCGG **GGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGATCGTTTTGGACTCTTTGGTG** CACCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGACGAGAACCTAAAACAGTTCC GCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTGTTTCTGTATTTGTCTGAAAATA TCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTGACCTTAGGTCACTGGAAAGATG TCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAAGAAGAGACGTTGGGTTACCTTCT GCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGCCGCGAGACGGCACCTTTAACCGAG ACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCACCTGGCCCGCATGGACACCCAGACC CCTTTGTACACCCTAAGCCTCCGCCTCCTCTTCCTCCATCCGCCCCGTCTCTCCCCCTTG **AACCTCCTCGTTCGACCCCGCCTCGATCCTCCCTTTATCCAGCCCTCACTCCTTCTCTAG** GCGCCCCCATATGGCCATATGAGATCTTATATGGGGCACCCCCGCCCCTTGTAAACTTCC CTGACCCTGACATGACAAGAGTTACTAACAGCCCCTCTCTCCAAGCTCACTTACAGGCTC TCTACTTAGTCCAGCACGAAGTCTGGAGACCTCTGGCGGCAGCCTACCAAGAACAACTGG ACCGACCGGTGGTACCTCACCCTTACCGAGTCGGCGACACAGTGTGGGTCCGCCGACACC **AGACTAAGAACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCCTGCTGACCACCCCCA** CCGCCCTCAAAGTAGACGGCATCGCGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGA CCCCGGGGGTGGACCATCCTCTAGACTGCCGGATCTCGAGGGATCCACCACCATGGACCC 

FIG.\_11A-1

GGTTATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGGGCCCGGAAACCTGGCCCTG TCTTCTTGACGAGCATTCCTAGGGGTCTTTCCCCTCTCGCCAAAGGAATGCAAGGTCTGT TGAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTGAAGACAACAACGTCTGTAG CGACCCTTTGCAGGCAGCGGAACCCCCCCCCCCGCGACAGGTGCCTCTGCGGCCAAAAGC CACGTGTATAAGATACACCTGCAAAGGCGGCACAACCCCAGTGCCACGTTGTGAGTTGGA TAGTTGTGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTCAACAAGGGGCTGAAGGATG CCCAGAAGGTACCCCATTGTATGGGATCTGATCTGGGGCCTCGGTGCACATGCTTTACAT GTGTTTAGTCGAGGTTAAAAAACGTCTAGGCCCCCGAACCACGGGGACGTGGTTTTCCT TTGAAAAACACGATGATAATATGGGGGGATCCACCGGTCGCCACCATGGTGAGCAAGGGCG AGGAGCTGTTCACCGGGGTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCC ACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGA **AGTTCATCTGCACCACCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGA** CCTACGGCGTGCAGTGCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCA **AGTCCGCCATGCCCGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCA** ACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGC TGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACT ACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACT TCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGA ACACCCCCATCGGCGACGGCCCCGTGCTGCCCGACAACCACTACCTGAGCACCCAGT CCGCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGA CCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAGTAAAGCGGCCGCTCGACGA TAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGGAATGAAAGACCCCACCTGTA GGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGA GAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACA GGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTG **AATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAA** CAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTC CAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTCG CTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCC TCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAA ACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGA GTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGTCTCGCTGCCTTGG GAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCACATGCAGCATGTAT **CAAAATTAATTTGGTTTTTTTTTCTTAAGTATTTACATTAAATGGCCATAGTTGCATTAAT** GAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCTCTTCCGCTTCCTCGCT GGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGG CCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCG CCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGG **ACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGAC** CCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCA TAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGT GCACGAACCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTC CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCACTGGTAACAGGATTAGCAG AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACAC

FIG.\_11A-2

TAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGT **GCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTCTACGGG** GTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAA TATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTC **AGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC** GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCCGAGCGCAGAAGTGG TCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAG TAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTC ACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTÂC **ATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAG AAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTAC** TGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTG AGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAACACGGGATAATACCGC GCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACT CTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTG **ATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAA TCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATG** TATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTC

FIG.\_11A-3

1-845 CMVpromoter/R/U5 5' LTR
1322 GAG ATG-ATC mutation
850-2100 extended \( \psi \) r gion
2151-2865 GFP coding region
2866-2894 GGGSGGG linker
2895-2952 FMDV 2a cleavage sequence
2953-3004 Bstx1/Bstx1/HinD3/Hpa1/Sal1/Not1 polylinker
3052-3645 3' LTR
3652-5715 pGEM backbone (pUC origin, ampR)

**ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATC** CCAAACTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATC **AATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGG** TATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTT ACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTA TTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGG GACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG GTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTC TCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCA **AAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGA** GGTCTATATAAGCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTC CTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCA TCCGACTTGTGGTCTCCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGT CAGCGGGGGTCTTTCATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACC TAGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGT ATCTGGCGGACCCGTGGTGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAG ACGTCCCAGGGACTTCGGGGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGAT CGTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGATATGTGGTTCTGGTAGGAGA CGAGAACCTAAAACAGTTCCCGCCTCCGTCTGAATTTTTGCTTTCGGTTTGGGACCGAA TTTCTGTATTTGTCTGAAAATATCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTT GACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCA AGAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGG CCGCGAGACGCCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTC ACCTGGCCCGCATGGACACCCAGACCAGGTCCCCTACATCGTGACCTGGGAAGCCTTGG CTTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCCTCCGCCTCCTCTT CCTCCATCCGCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTCGATCCTC CCTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTAT ATGGGGCACCCCCCCCTTGTAAACTTCCCTGACCCTGACATGACAAGAGTTACTAAC AGCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAG GAGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGG AAAGGACCTTACACAGTCCTGCTGACCACCCCCACCGCCCTCAAAGTAGACGGCATCGC **AGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTA** GACTGCCGGATCTCGAGGGATCCACCATGGTGAGCAAGGGCGAGGAGCTGTTCACCGGG

FIG.\_11B-1

GTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTC CGGCGAGGGCGAGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCA CCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGACCTACGGCGTGCAG TGCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCC CGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCC GCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATC GACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACTACAACAGCCA CAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACTTCAAGATCC GCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAACACCCCC ATCGGCGACGGCCCCGTGCTGCCCCGACAACCACTACCTGAGCACCCAGTCCGCCCT GAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCG CCGGGATCACTCTCGGCATGGACGAGCTGTACAAGGAATTCGGAGGTGGCAGCGGTGGC GGTCAGCTGTTGAATTTTGACCTTCTTAAACTTGCGGGAGACGTCGAGTCCAACCCTGG GCCCACCACCATGGAAGCTTCCATTAAATTGGTTAACGTCGACGCGGCCGCTCGAC GATAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGGGAATGAAAGACCCCACCT GTAGGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAA CTGAGAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCC AAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCCAAGAACAGATGGAA CAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGG CCAAGAACAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCA GATGTTTCCAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCA ATCAGTTCGCTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGC CCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGT **GTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAG** GGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGT CTCGCTGCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCA **CATGCAGCATGTATCAAAATTAATTTGGTTTTTTTTTTCTTAAGTATTTACATTAAATGGC** CATAGTTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCT CTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTA TCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAA GAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGG CGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG **AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCT** CGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCCTT CGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC GTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTT ATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAG CAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTG **AAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCT** CAAGAAGATCCTTTGATCTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACG TTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATT **AAAAATGAAGTTTGCGCAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGT** TACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCAT **AGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCC** CCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATA

FIG.\_11B-3

1-845 CMVpormoter/R/U5 5' LTR
1322 GAG ATG-ATC mutation
850-2100 extended ψ region
2146-2173 two Bstx1 peptide cloning sites
2173-2214 EoR1/Apa1/Hpa1/Not1 polylinker
2262-2855 3' LTR
2855-4901 pGEM backbone (pUC origin, ampR)

**ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATC** CCAAACTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATC **AATTACGGGGTCATTAGTTCATAGCCATATATGGAGTTCCGCGTTACATAACTTACGGT AAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGT ATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTA** CGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTAT TGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCCAGTACATGACCTTATGGG **ACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGG** TTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCT CCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAA **AATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGAG** GTCTATATAAGCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTCC TCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCAT CCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTC AGCGGGGGTCTTTCATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCA **AGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGTA** TCTGGCGGACCCGTGGTGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAGA CGTCCCAGGGACTTCGGGGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGATC GTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGAC GAGAACCTAAAACAGTTCCCGCCTCCGTCTGAATTTTTGCTTTCGGTTTGGGACCGAAG TTCTGTATTTGTCTGAAAATATCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTG **ACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAA** GAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGC CGCGAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCA CCTGGCCCGCATGGACACCCAGACCAGGTCCCCTACATCGTGACCTGGGAAGCCTTGGC TTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCCTCCGCCTCCTCTTC CTCCATCCGCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTCGATCCTCC CTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTATA TGGGGCACCCCGCCCCTTGTAAACTTCCCTGACCCTGACATGACAAGAGTTACTAACA GCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAGA CCTCTGGCGGCAGCCTACCAAGAACAACTGGACCGACCGGTGGTACCTCACCCTTACCG AGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGGA **AAGGACCTTACACAGTCCTGCTGACCACCCCCACCGCCTCAAAGTAGACGGCATCGCA** GCTTGGATACACGCCGCCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTAG **ACTGCCGGATCTCGAGGGATCCACCACCATGGACCCCCATTAAATTGGAATTCGGGGCC** TAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGAGAATAGAGAAGTTCAGATCA

FIG.\_11C-1

AGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAG TTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTGAATATGGGCCAAACAGGA TATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGTCCCCAGATG CGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTCCAGGGTGCCCCAAGGA CCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTCGCTTCTCGCTTCTGTT CGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCC **AGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGT** TGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTAC CCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGTCTCGCTGCCTTGGGAGGGTCTCCT CTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCACATGCAGCATGTATCAAAATTAAT TTGGTTTTTTTTTTTAAGTATTTACATTAAATGGCCATAGTTGCATTAATGAATCGGCC **AACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCTCTTCCGCTTCCTCGCTCACTGACT** CGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCA **AAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCC** CTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTA TAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCT GCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATA GCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTG CACGAACCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTC CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCA GAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAC **ACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAG** GCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCT ACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATT **ATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTGCGCAAATCAA** TCTAAAGTATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCA CCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTA GATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAG CGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGA **AGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAG** TCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCC TCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCAC TGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTC **AACACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAAC GTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAA** CCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTG AGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTT GAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTC ATGACATTAACCTATAAAAATAGGCGT

FIG.\_11C-2

(1) C12ScFas Survival construct

C12ScFas: epsilon-cFas(CD95)-Ires-Hygro-BGH PolyA put into C12s vector backwards so that no leaky transcription happens through the cmv promoter

oget ggaaaggaeet tacacagteet gget gaccaceececacegeet caaagtagaeggeat egeaget t ggatacaege cgcccacgtgaaggctgccgaccccggggggtggaccatctctagactgccGGATCTCGAGGATCCTCCCCAGCATGCC tgtctctgtctgactgtgtttctgtatttgtctgaaaatatgggcccgggccagactgttaccactcccttaagtttgac cgttacataacttacggtaaatggcccgcctggctgaccgcccaacgacccccgcccattgacgtcaataatgacgtatg agtacatcaatgggcgtggatagcggtttgactcacggggatttccaagtctccaccccattgacgtcaatgggagtttg gagtegecegggtaceegtgtatecaataaaeeetettgeagttgeateegaettgtggtetegetggttetegtteettgggaaggg teteetetgagtgattgaetaccegteagegggggtettteatttggggggetegteeggggategggagacceetgeeeag ttttatgegeetgegtegtaetagttagetaactagetetgtatetggegggeeeegtggtggaactgaeggtteggaa caccoggcogcaaccotgggagacgtcccagggacttcgggggccgttttgtgggcccgacctgagtccaaaaatcccga tegttttggactetttggtgeaceeecttagaggagggatatgtggttetggtaggagaegagaacetaaaacagttee cttaggtcactggaaagatgtcgagcggatcgctcacaaccagtcggtagatgtcaagaagagacgttgggttaccttct gctctgcagaatggccaacctttaacgtcggatggccgcgagacggcacctttaaccgagacctcatcaccaggttaag atcaaggtetttteaeetggeeegeatggaeaeecaggaeagaeaggteeettaeategtgaeetgggaageettggettttga aaceteetegttegaeceegeetegateeteeetttateeageeeteaeteettetetaggegeeeeeatatggeeatat gagatettatatggggeaeeeeegeeeettgtaaaetteeetgaeeetgaeatgaeatgaeagagttaetaaeageeeetetet ccaageteaettacaggetetetaettagtecageaegaagtetggagaeetetggeggeageetaeeaagaaeaaetgg accgaccggtggtacctcacccttaccgagtcggcgacacagtgtgggtccgccgacaccagactaagaacctagaacct atcacgaggccctttcgtcttcaagaacagctttgctcttaggagtttcctaatacatcccaaactcaaatatataaagc atttgacttgttctatgccctagttattaatagtaatcaattacggggtcattagttcatagcccatatatggagttccg ttcccatagtaacgccaatagggactttccattgacgtcaatgggtggagtatttacggtaaactgcccacttggcagta catcaagtgtatcatatgccaagtacgccccctattgacgtcaatgacggtaaatggcccgcctggcattatgcccagta catgacettatgggaettteetaettggcagtacatetaegtattagteetegetattaeeatggtgatgeggtttttgge ttttggcaccaaaatcaacgggactttccaaaatgtcgtaacaactccgccccattgacgcaaatgggcggtaggcatgt 

FIG.\_12A

GCAAACAACAGATGGCTGGCAACTAGAAGGCACAGTCGAGGtCTAGCTTGCCAAACCTACAGGTGGGGTCTTTCATTCCC

tgacaccattctttcgaacaaagcctttaacttgacttagtgtcatgactccagcaatagtggtgatatatttactcaag tcaacatcagataaatttattgccactgtttcaggatttaaggttggagattcatgagaaccttggttttcctgtg ctttctgcatgttttctgtacttcctttcttctcaccaaacaattagtggaattggcaaaagaagaagacaagccacc TTTTTACCAGGTTGGCATGGTTGACAGCAAAATGGGCCTCCTTGATAATCCTTCTGAGCAGTTTTTATCAGTTTTCATG CCCTTTTTCTGGAGACTAAATAAAATCTTTTATTTTAtcgatagatcccggtcggcatctactctattcctttgccctcg gacgagtgctgggggggtttccactatcggcgagtacttctacacagccatcggtccagacggcggctctgcgg gogatttgtgtacgcccgacagtcccggctccggatcggacgattgcgtcgcatcgaccctgcgcccaagctgcatcatc gaaattgccgtcaaccaagctctgatagagttggtcaagaccaatgcggagcatatacgcccggagccgcgggggtctctg gegaeetegtattgggaateeeegaacategeetegeteeagteaatgaeegetgttatgeggeeattgteeggae attgttggagccgaaatccgcgtgcacgaggtgccggacttcggggcagtcctcggcccaaagcatcagctcatcgagag cctgcgcgacggacgcactgacggtgtcgtccatcacagttttgccagtgatacacatggggatcagcaatcgcgcatatg aaatcacgccatgtagtgtattgaccgattccttgcggtccgaatgggccgaacccgctcgtctggctaagatcggccgc cctgtgcacggcgggagatgcaataggtcaggctctcgctaaattccccaatgtcaagcacttccggaatcgggagcgcg geegatgeaaagtgeegataaacataacgatetttgtagaaaceateggegegeagetatttaeeegeaggaeatateeaeg cectectacategaagetgaaageacgagattettegeceteegagagetgeateaggteggagaegetgtegaaetttt cgatcagaaacttctcgacagacgtcgcggtgagttcaggctttttcatggtattatcatcgtgtttttcaaaggaaaac cacgtccccgtggttccggggggcctagacgttttttaacctcgactaaacacatgtaaagcatgtgcaccgaggccccag atcagatcccatacaatggggtaccttctgggcatccttcagccccttgttgaatacgcttgaggaggccatttgactc tttccacaactatccaactcacaacgtggcactggggttgtgccgcctttgcaggtgtatcttatacacgtggcttttgg cogcagaggcacctgtcgccaggtggggggttccgctgcaaagggtcgctacagacgttgttgtttttcaagaagc **ELCCAGAGGAACTGCTTCCTTCACGACATTCAACAGACCTTGCATTCCTTTGGGGGAGGGGGAAAGACCCCL**agactaga ccaagctttggatttcatttctgaagtttgaattttctgagtcactagtaatgtccttgaggatgatagtctgaattttc tctgcaagagtacaaagattggcttttttgagatctttaatcaatgtgtcatacgcttcttctttccatgaagttgatg ccaattacgaagcagttgaactttctgttctgctgtgtgtcttggacattgtcattcttgatctcatctattttggcttcat **ccaaccggTTTCTGGGACTTTGTTTCCTGCAGTTTGTATTGCTGGTTGCTGTGCATGGCTCAAGGGTTCCATGTTCACA GAGGCGCAGCGAACACACAGTGTTCACAGCCAGGAGAATCGCAGTAGAAGTCTGGTTTGCACTTGCACTTGGTATTCTGGGT CAGGGTGCAGTTTGTTTCCACTTCTAAACCATGCTCTTCATCGCAGAGTGTGCATCTTCTGCATTTATCAGCATAATGGT** 

FIG.\_ 12B

GIGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCC TTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGGGGGGGAGAGGGCGGTTTGCGTATTGGGCG **ATGGAACAGGCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCG** GGCCATagtttcGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACATACGAG TAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAAGGCCAGCAAAAGGCCAGGAACCGT <u>AAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAAGT</u> CTAGCTTAAGTAACCCATTTTGCAAGGCATGGAAAAATACATAACTGAGAATAGAGAAGTTCAGATCAAGGTCGGAACAG TGTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGA CTACCCGTCAGCGGGGGTCTTCAcatgcaGCATGTATCAAAATTAATTTGGTTTTTTTTTTTTTAAGTATTTACATTAAAT GCTGTAATTGAACCTGGGAGTGGACACCTGTGGAGAAAAGGCAAAGTGGATGTCAGTAAGACCAATAGGTGCCTATCAG cccgggccgccctggaagttcccttttctctctgttcttgggaagtcgattgagcaacagcggggggtcaggtgaggctcc ttcactaccgatgcacaccgagtgctGggggaggttctctctctctcaggcccaacCccagggccctgcctaggtccc ctgtgacccgcttggagctggcaccctgagtggcctcacCTTGTACTCCCAGGTCACTGTCtcgacGCGGCC GCTCGAcgataaaataaaagattttatttagtctccagaaaaaggggggaatgaaagaccccacctgtaggtttggcaag CCAGAGGCAGGACAGCCCAGATCCACACCATGGTGGCTTTACCAACAGTACCGGAATGCCAAGCTTGCGGCCGCTTAAGA aaacgcaagagtcttctctgtctcgacaagcccagtttctattggtctccttaaacctgtcttgtcttgtaaccttgatac CTGCCCAGTGCCTCACGACCAACTTctgcaggaattcctggacagctcccagatgatcagtaaccgtggttgttatttct gtgccgggcagtggagcctgggtagggggagctctgcctcagtgctttcagctaaaaatggggtgggaaccccCaggagg ggactetCaetettgaegeatgegtggettggtggteceagteageaaaettggggteeegttgeetgggaaagggagag

CCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCAC aatagtgtatgcggcgaccgagttgctcttgcccggcgtcaacacggggataataccgcgcccacatagcagaactttaaaa gtgotcatcattggaaaaacgttottcggggcgaaaactotcaaggatottaccgotgttgagatccagttcgatgtaacc cactegigeacceaacigateticageatetitaetiteaceagegitetetgggigageaaaaggaaggeaaatg CAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATAGTTGCCTGACTCCCGGCCGTCGTGTAGATAACTACGA GCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAA **ACTGCATAATTCTCTTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGagtactcaaccaagtcattctgag** <u> AGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGG</u> **TAACTATCGTCTTGAGTCCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCACTGGTAACAGGATTAGCAGA** TGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTTTTACGGGGT CTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTT **TTAAATTAAAAATGAAGTTTGCGCAAATCAATCTAAAGTATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAAT** <u>TACGGGAGGGCTTACCATCTGGCCCCCAGTGCTGCAATGATACCGCGAGACCCCACGCTCACCGGCTCCAGATTTATCAGCA</u> cogcaaaaaagggaataagggogacacggaaatgttgaatactcatactcttccttttcaatattattgaagcatttat **CGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACAACTAGAAGGACAGTATTTGGTATC** cagggttattgtctcatgacattaacctataaaaataggcgt

TGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTC

2.) Ahhhh: epsilon-cFas' (CD8 or mLyt2)-Ires-Hygro-BGHpolyA also in C12s backwards

(2) Ahhhh: Survival construct

cgctggaaaggaccttacacagtcctgctgaccacccccaccgccctcaaagtagacggcatcgcagcttggatacacgc cgcccacgtgaaggctgccgaccccgggggtggaccatcctctagactgccGGATCTCGAGGATCCTCCCCAGCATGCC catgaccttatgggactttcctacttggcagtacatctacgtattagtcatcgctattaccatggtgatgcggttttggc tetectetgagtgattgaetaceegteagegggggtettteatttggggggetegteeggggategggagaeceetgeeeag ttttatgegeetgegtegtaetagttagetaaetagetetgtatetggeggeeeegtggtggaaetgaegatteggaa cacceggcegeaaceetgggagaegteecagggaettegggggeegtttttgtgggeeegaeetgagteeaaaateeega tegttttggaetetttggtgeaceeeettagaggagggatatgtggttetggtaggagaegagaacetaaaaacagttee tgtctctgtctgactgtgtttctgtatttgtctgaaaatatgggcccgggccagactgttaccactcccttaagtttgac cttaggtcactggaaagatgtcgagcggatcgctcacaaccagtcggtagatgtcaagaagaagacgttgggttaccttct getetgeagaatggecaacetttaacgteggatggeegegagaeggeacetttaaeegagaeeteateaggttaag atcaaggtetttteaeetggeeegeatggaeaeeceagaeeaggteeeetaeategtgaeetgggaageettggettttga coccetecetgggtcaageeetttgtacaecetaageeteegeeteetetteeteeateegeeeegteteeteeettg aacetectegttegaeceegeetegateeteeetttateeageeeteaeteettetetaggegeeeeeatatggeeatat ccaageteaettacaggetetetaettagtecageaegaagtetggagaeetetggeggeageetaeeaagaaeaaetgg accgaccggtggtacctcacccttaccgagtcggcgacacagtgtgggtccgccgacaccagactaagaacctagaacct cgttacataacttacggtaaatggcccgcctggctgaccgcccaacgaccccgcccattgacgtcaataatgacgtatg ttoccatagtaacgccaatagggactttocattgacgtcaatgggtggagtatttacggtaaactgcccacttggcagta catcaagtgtatcatatgccaagtacgccccctattgacgtcaatgacggtaaatggcccgcctggcattatgcccagta agtacatcaatgggcgtggatagcggtttgactcacggggatttccaagtctccaccccattgacgtcaatgggagtttg gagtegecegggtaceegtgtateeaataaaceetettgeagttgeateegaettgtggtetegetgtteettggggaggg atcacgaggccctttcgtcttcaagaacagctttgctcttaggagtttcctaatacatcccaaactcaaatatataaagc atttgacttgttctatgccctagttattaatagtaatcaattacggggtcattagttcatagcccatatatggagttccg ttttggcaccaaaatcaacgggactttccaaaatgtcgtaacaactccgccccattgacgcaaatgggcggtaggcatgt

GCAAACAACAGATGGCTGGCAACTAGAAGGCACAGTCGAGGtCTAGCTTGCCAAACCTACAGGTGGGGTCTTTCATTCCC

gegaectegtattgggaateecegaacategeetegeteeagteaatgaeegetgttatgeggeeattgteegteaggae attgttggagccgaaatccgcgtgcacgaggtgccggacttcggggcagtcctcggcccaaagcatcagctcatcgagag cctgcgcgacggacgcactgacggtgtcgtccatcacagtttgccagtgatacacatggggatcagcaatcgcgcatatg aaatcacgccatgtagtgtattgaccgattccttgcggtccgaatgggccgaacccgctcgtctggctaagatcggccgc agogatogoatocatggcotocgogacoggotgcagaacagogggcagttoggtttcagggcaggtcttgcaacgtgacac cctgtgcacggcgggagatgcaataggtcaggctctcgctaaattccccaatgtcaagcacttccggaatcgggagcgcg googatgoaaagtgoogataaacataacgatotttgtagaaaccatcggogoagctatttaccogoaggacatatocacg cgatcagaaacttctcgacagacgtcgcggtgagttcaggctttttcatggtattatcatcgtgtttttcaaaggaaaac cacgtccccgtggttccggggggcctagacgtttttaacctcgactaaacacatgtaaagcatgtgcaccgaggccccag atcagatcccatacaatggggtaccttctgggcatccttcagccccttgttgaatacgcttgaggaggccatttgactc tttccacaactatccaactcacaacgtggcactggggttgtgccgcctttgcaggtgtatcttatacacgtggcttttgg **ttccagaggaactgcttccttcacgacattcacagaccttgcattcctttgcattcgtttgcgagagggggaaagactaga** gaaattgeegteaaceaagetetgatagagttggteaagaceaatgeggageatataegeeeggageegegggggagteetg caageteeggatgeeteegetegaagtagegegtetgetgeteeatacaageeaageaaeggeeteeagaagaagatgttg ccetcctacatcgaagctgaaagcacgagattcttcgccctccgagagctgcatcaggtcggagacgctgtcgaactttt gacgagtgctgggggcgtcggtttccactatcggcgagtacttctacacagccatcggtccagacggccgcgcttctgcgg

CCCTTTTTCTGGAGACTAAATAAATCTTTTATTTTA tega taga teeegg teggea tetae tetat teet tige eeteg

ccaagctttggatttcatttctgaagtttgaattttctgagtcactagtaatgtccttgaggatgatagtctggaattttc totgcaagagtacaaagattggcttttttgagatctttaatcaatgtgtcatacgcttcttctttccatgaagttgatg ccaattacgaagcagttgaactttctgttctgctgtgtgtcttggacattgtcattcttgatctcatctattttggcttcat tgacaccattctttcgaacaaagcctttaacttgacttagtgtcatgactccagcaatagtggtgatatatttactcaag tcaacatcagataaatttattgccactgtttcaggatttaaggttggagattcatgagaaccttggttttcctttctgtg ctttctgcatgttttctgtacttcctttctcttcacccaaacaattagtggaattggcaaaagaagaagacaaagccacc ccaaccggtttccggtccccttcactgagccacggggccgacaatcttctggtctctggggctgagatgtcccggtaggg tgcacaggtgagggagttcgcagcactggcttggtagtagtagagttcactttctgaaggactggcacgacagaactgaa gtacatcaccgagttgctgatgactgagcagaaatagtagccttcgttttccttgctgaacttgttcagggtgagaacgt acttattattcgtgtccctcatggcagaaaacagtttcgacgaattcagcttctcgtcccacgttatcttgttgtgggat gaagccatatagacaacgaaggtgggctgggggggggtttggagctggagttctggaagtgccaagagccatccttgcgaaac ggaccccaacacttcacataccaggtccaccttctgaccaagttcggcgtccattttctttggaaagattcggagttcgg gtgcctgtggcttagcttctccactccccaggataatcgactcacccagcagcagcaggttcagcgacagaaagcgggtc aacggtgaggccatgGTGGCTTTACCAACAGTACCGGAATGCCAAGCTTGCGGCCGCTTAAGAGCTGTAATTGAACCTGG

GAGTGGACACCTGTGGAGAAAGGCAAAGTGGATGTCAGTAAGACCAATAGGTGCCTATCAGAAACGCAAGAGTCTTCT

CTGTCTCGACAAGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGATACTTACCTGCCCAGTGCCTCACG

CTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGG

TCTTTCAcatgcaGCATGTATCAAAATTAATTTGGTTTTTTTTTTTTAAGTATTTACATTAAATGGCCATagtttcGTAAT

CATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGT

TTTTGCAAGGCATGGAAAATACATAACTGAGAATAGAGAAGTTCAGATCAAGGTCGGAACAGATGGAACAGGCAATAAA

**AGAGCCCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCT** 

**ACCAACTTctgcaggaattcctggacagctcccagatgatcagtaaccgtggttgttatttctgtgccgggcagtggagc** ctgggtagggggagctctgcctcagtgctttcagctaaaaatggggtgggaaccccCaggaggcccgggccgcctggaa gttcccttttctctctctgttcttgggaagtcgattgagcaacagcgggggtcaggtgaggctccttcactaccgatgcaca ccgagtgetGgggggaggtteteteteteteaggeceaaeCeeagggeeeetgeetaggteeeggaetetCaetettgae gcatgcgtggcttggtggtcccagtcagcaaacttggggtcccgttgcctgggaaagggagagagggtactgggcatcgacg cctctgcttccacgaaagccttgtgaagaaaggatgggggcgcttttgtgcaggagaatgaggcgcactgaggtgaactg gccctcgggggcgcgtgtcccagatgtgtgtgtgcagggcctcctgatggccgcagccctcgtccctgtgacccgcttggag ctggcacctgagtggcctcacCTTGTACTCCCAGGTCACTGTCtcgacGCGGCCGCTCGAcgatAAATAA

GGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAG CCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCACTGGTAACAGGATTAGCAGAGGGGTATGTAGGCGGT GACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGGCTTACCGGATAC GTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGGGGAGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGC gaatcaggggataacgcaggaaagaacatgtgagcaaaaaggccagcaaaaaggccagcaaggaaccgtaaaaaggccgcgttgct CTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGT <u>aaagcctggggtgcctaatgagtgagctaactcacattaattgcgttgcgctcactgcccgctttccagtcggaaacct</u> TCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGT

GTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATG **CTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGagtactcaaccaagtcattctgagaatagtgtatgcggcga** ccgagttgctcttgcccggcgtcaacacgggataataaccgcgccacatagcagaactttaaaagtgctcatcattggaaa acgttetteggggggaaaaeteteaaggatettaccgetgttgagatecagttegatgtaaeecaetegtgeaeeeaet gatottcagcatottttaotttcaccagcgtttctgggtgagcaaaaacaggaaggcaaaatgccgcaaaaagggaata agggegacacggaaatgttgaatactcatactcttccttttcaatattattgaagcatttatcagggttattgtctcat CGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTTA gacattaacctataaaaataggcgt

**AGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAAC** 

GCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCC

GAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTAAAATTAAAATGAAG

TTTGCGCAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCT

CAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCA

# FIG.\_ 13D